out, many are tamponed or given ergot until the undiagnosed cancer is hopeless.

A more serious neglect, and one for which there is no excuse, is the treatment by radium or x-ray of a bleeding uterus before an accurate diagnosis is made. The radium dose and number of applications is, of course, dependent upon the existing pathology. As to whether x-ray should be used of course depends upon an accurate diagnosis. Still we all see patients so treated without diagnostic curettage having been done who were given the customary dose for what was thought to be a small myoma or polyp and later were found to have a hopeless and neglected cancer. The physician who treats a uterus with radium or x-ray should know exactly what he is treating, as it is certainly a very great responsibility.

I saw, not long ago, a doctor's wife who began to bleed one year after her menopause. Diagnosis was made of a moderate sized myoma, which was treated with radium. The bleeding stopped for six months. Later a large and hopeless ovarian cancer was removed. The bleeding in this case had been stimulated by the ovarian growth, as mentioned by Doctor Schulze; and in this case if an accurate diagnosis could have been made and operation immediately done, her chances certainly would have been much better.

Doctor Schulze has found that two-thirds of those women showing bleeding after the menopause had cancer of the genital tract. This being true, certainly a careful investigation should be made before any treatment is undertaken.

H. N. Shaw, M. D. (901-902 Pacific Mutual Building, Los Angeles).—I wish to emphasize the fact that, while diagnostic curettage is almost always indicated in these individuals, precautions must be observed. I shall cite two cases as examples.

Case 1.—M. R., age sixty-five, single, virgin. Complaint: slight vaginal bleeding for two weeks, thirteen years after menopause. On June 8, 1929, frozen section of curettings showed fundus carcinoma of "low malignancy" and panhysterectomy was performed at once. Five months later, on November 3, the patient had a vaginal hemorrhage. At examination that day, introduction of a speculum broke off a vascular tumor 3 by 1 by 1 centimeters at the upper angle of the vagina. Frozen section showed highly malignant tumor. There were two slightly smaller tumors in the upper vagina. These were given two applications of radium, and the patient had no recurrences.

Carcinoma rarely implants on mucous surfaces. We felt that the routine vaginal scrubbing with iodin and alcohol had removed the surface epithelium and laid open raw surfaces on which the carcinomatous fragments could implant. To avoid this danger in elderly patients with thin mucosa, we advise great care in the vaginal cleaning.

Case 2.—E. B., age fifty-seven, single, virgin. Complaint: Painless bleeding for two weeks nine years after menopause.

Curettage, August 30, 1928. Frozen section unsatisfactory, but rush paraffin section twenty-four hours later showed fundus carcinoma. On September 1, panhysterectomy showed a papillary carcinoma in upper angle of fundus two centimeters in diameter on a small pedicle.

This patient came into the hospital within less than three years, with signs of intestinal obstruction, and died on July 6, 1931. Autopsy showed carcinoma scattered over peritoneum and intestinal walls, causing obstruction, but no tumors in the broad ligaments, the usual site of recurrence.

An early carcinoma of the fundus in an elderly woman is usually cured by hysterectomy. We felt that the recurrences were due to material squeezed out through the tubes during the hysterectomy, rather than metastatic invasion by the lymphatics.

In any case of hysterectomy where carcinoma of the fundus is expected, the tubes should be ligated before exerting pressure on the fundus. This is especially necessary where a preliminary curettage has been done.

Doctor Schulze (Closing).—A statistical study such as the one above submitted serves mainly to reëmphasize the importance of facts which are well known to us all. Since in two-thirds of all cases, including those with only the slightest spotting, postmenopausal bleeding is due to malignancy of the genital tract, it is not a symptom which can ever with safety be treated expectantly. As both Doctor Craig and Doctor Sperry have pointed out, the important thing is to establish a diagnosis. We may thus avoid, on the one hand, over-radical treatment in elderly patients who may be very poor operative risks, or, on the other hand, avoid palliative treatment with medication or inadequate radiation when we are dealing with cancer. The details of technique which Doctor Shaw has emphasized are most important, for without this great care to prevent dissemination at the time of operation, we may merely hasten the fatal termination rather than cure by our operative procedure.

CIRCULATION AND POSTURAL CHANGE*

ADJUSTMENTS IN HEALTH AND DISEASE

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ADJUSTMENT of the circulation to oppose the effect of gravity on assumption of the upright posture is largely dependent upon the phenomena of peripheral blood pressure. The three main factors contributing to a given blood pressure level are: (1) heart output; (2) blood volume; and (3) peripheral resistance. Defect in any of these factors may result in inefficient postural adjustment by the circulation.

The heart output, according to Grollman,[1] does not vary in normal subjects on change from recumbency to standing. The syncope associated with Stokes-Adams syndrome, however, represents failure of postural adjustment as a result of cardiac inefficiency. The animal experiments of Piorry in 1826 are quoted by Hill [2] as proving the importance of an adequate blood volume in compensating the effect of gravity.

PHYSIOLOGIC ADJUSTMENT OF PERIPHERAL RESISTANCE TO POSTURAL CHANGE

Definite information regarding the physiologic adjustment of peripheral resistance to postural change dates from the experimental work of Hill,[2] and Hill and Barnard [3] in 1895 and 1897 respectively. From their experiments on animals, these investigators showed that compensatory constriction of the splanchnic arterioles successfully opposes the effect of gravity and prevents the development of cerebral anemia during the maintenance of the upright posture. Section of the splanchnic nerves, which abolished vasomotor tone in the splanchnic area, resulted in dilatation of the arterioles in this region. This caused little or no embarrassment to the circulation while the horizontal posture was maintained, on account of increased respiratory movements and abdominal muscle tone being capable of compensating for the arteriole dilatation. Assump-

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tion of the erect posture, however, resulted in shift of the blood mass to the splanchnic venules and veins. Even under these conditions, the experimental animals were nevertheless capable of maintaining a fractional amount of venous return to the heart by increased force of respiratory movements which resulted in considerable aspiration of blood from the splanchnic area of venous congestion. After section of the spinal cord at the level of the first dorsal vertebra, efferent impulses were cut off from the vasomotor and respiratory centers, and compensation for the effect of gravity failed. Under these latter conditions, however, external pressure and massage of the abdomen appeared capable of opposing collection of the blood mass in the splanchnic area. After vagus section, failure of the heart to decrease its rate on attaining the horizontal position proved the importance of vagus control of heart rate in postural adjustment.

PARALYSIS OF SPLANCHNIC VASOCONSTRICTORS

Moderate ether anesthesia was shown by Hill [2] not to interfere with circulatory compensation for the upright posture. The forcing of ether or chloroform anesthesia was found to damage the compensation for postural change for a considerable period of time after the anesthetics had been removed. A paralysis of the vasomotor center took place with the pushing of both ether and chloroform. The latter anesthetic, however, depressed the vasomotor center more quickly and, in addition, depressed the heart. Therefore that investigator warned that chloroform could kill a patient when the abdomen is lower than the heart. Hill's demonstration of increased respiratory movements being capable of compensating for lack of splanchnic vasomotor tone in the upright posture probably explains why spinal anesthesia, when confined in motor paralysis to a level below the innervation of the major respiratory muscles, interferes but little with circulatory efficiency.

Other causes for paralysis of the splanchnic vasoconstrictors were named by Hill as follows: (1) severe operative procedures; (2) excessive handling of the intestines; (3) spinal cord injuries; (4) asphyxia; and (5) poisons, such as curare. He further believed that reflex dilatation of the splanchnic arterioles characterizes ordinary emotional syncope in the human subject. Asthenic individuals were believed by him to be less capable of compensating for gravity and were more prone to syncopal attacks of the reflex type. In the treatment of this type of circulatory collapse, compression and elevation of the abdomen were recommended.

SHOCK

In correlating failure of splanchnic compensation for postural change with surgical and traumatic shock, it seems best to accept Cannon's [4] preference for classification of shock into primary and secondary types. Primary shock is that type which arises almost immediately after an injury, or suddenly during the course of an operation, and is apparently induced by reflex inhibition of the vasomotor center. The dilatation of the splanchnic arterioles and consequent venous engorgement which occurs in this type of shock probably represents the same phenomenon as obtains during failure of vasomotor tone to compensate for postural change. Elevation of the abdomen, with lowering of the head, has proved alleviative in the treatment of primary shock, emotional syncope and symptoms arising from failure to compensate for the effect which gravity exerts upon the circulation. These phenomena are quite different from secondary or delayed traumatic shock which Cannon conceives as being characterized by arteriole constriction, capillary stasis, and diffusion of plasma into the tissue spaces with resultant decrease of the total blood volume. Apparently the vasomotor tone is effectively maintained until a very late stage of secondary shock is reached; hence lowering of the head is incapable of alleviating this latter form of collapse.

EFFECTS OF POSTURAL CHANGE IN HUMAN SUBJECTS

In human subjects, the normal response of pulse and blood pressure to postural change has been carefully studied by various investigators.[5, 6, 7, 8] It is now quite generally accepted that a change from lying to standing posture in human subjects normally entails an average *rise* of ten to twelve beats in pulse rate, an average *rise* of from eight to ten millimeters diastolic blood pressure, and a very slight *fall* (0 to 4 millimeters) of the systolic blood pressure at the brachial artery region. This results in a decrease of approximately eight to twelve millimeters of pulse pressure on the assumption of the erect posture. Only very slight differences in the pulse and blood pressure reactions occur whether the postural change is actively or passively carried out. Raising of the head 45 degrees above horizontal was reported by Ellis [6] to incite approximately the same compensatory response as when the total change from horizontal to upright took place. Failure of the diastolic blood pressure to rise on standing has been interpreted by Sewell,[9] Mortenson [8] and others as indicating a lack of vasomotor tone in the human subject.

Turner,[10, 11, 12] in her study of the reactions of normal young women to prolonged standing, found that those individuals exhibiting a high reclining heart rate, or marked decrease of pulse pressure in the erect posture, were prone to develop symptoms of dizziness on prolonged standing. Her data suggests that better postural adjustment occurs in those subjects who do not give a previous history of faintness or dizziness on standing. She believes that abnormal rise of diastolic blood pressure on postural change indicates insufficiency of heart output. This investigator also shows that stagnation of blood in the abdominal area may occur during prolonged standing, and that bandage or support to the abdomen relieves the resultant symptoms. The improvement in postural adjustment after eating, reported by her, indicates the rôle which increased

intestinal peristalsis may play in augmenting venous return.

Since 1925, when Bradbury and Eggleston [13] reported three cases exhibiting marked fall of blood pressure on assumption of the upright posture, a total of eleven cases of true postural hypotension, without associated Addison's disease, has been reported in the literature. Review of these case reports reveals a high incidence of commonly associated phenomena such as syncopal attacks on change from lying to standing, slow, unchanging pulse rate on postural change, anhidrosis, slight decrease in the basal metabolic rate and loss of sex urge. Several of the older cases exhibited marked general arteriosclerosis, which may have been important in consideration of their etiology. Since Ghrist and Brown [14] report successful alleviation of symptoms in one case of true postural hypotension by repeated small doses of ephedrin, this drug deserves a trial in cases so diagnosed. Those cases obtaining relief of postural symptoms by use of ephedrin probably present an atony of the myoneural junctures of the arterioles as their primary defect. Other cases reveal more probable evidence of defect in the nervous system of vasomotor control. In this disease, failure of abdominal support to give symptomatic relief in practically all attempts at treatment by this measure, presents evidence that regions other than the splanchnic area may participate in the phenomenon of circulatory stasis on assumption of the upright posture.

In 1927, Ghrist and Rowntree [15] reported one case of Addison's disease which exhibited an associated postural hypotension. Since then Ghrist [16] has reported the postural reactions revealed by a series of ten cases of Addison's disease. In three (30 per cent) of these cases there occurred such marked fall of blood pressure and rise in pulse rate as to become incapable of determination, and symptoms of impending syncope were experienced as the upright posture was reached.* One other case of postural hypotension associated with Addison's disease was reported by Duggan and Barr [17] in 1931. The marked rise in pulse, associated with severe fall of blood pressure, differentiated these Addison's disease reactions to postural change from those of true postural hypotension cases similarly studied. Failure of epinephrin or ephedrin to relieve the postural collapse in the Addison's disease cases indicated that factors such as small heart size, general muscular weakness,† lack of circulating hormones from the suprarenal glands, etc., probably combine to prevent an efficient adjustment of the circulation to the upright posture. Marked fall of blood pressure on postural change was exhibited by no other individuals or groups of patients so studied.

Postural tests carried out by Ghrist [16] on other groups of patients present evidence that neither essential hypotension nor undernourishment preclude normal response of pulse and blood pressure to postural change. Also, subnormal rise of diastolic blood pressure (without resultant symptoms) on passive change from horizontal to erect was exhibited by groups of patients with scleroderma, chronic infectious arthritis, and benign (essential) hypertension. The group of ten cases of malignant (essential) hypertension showed marked tendency to diastolic fixation in all postures. Patients with complaints of general weakness were shown capable of initiating normal postural response, but often yielded evidence of fatigue in their mechanism after several minutes' normal maintenance of this function. Symptoms on postural change were seldom produced unless a previous history of this association could be elicited from the patient. Postural studies before and after operation indicated that neither lumbar, nor cervico-thoracic sympathetic ganglionectomy and trunk resection appreciably altered the reaction of diastolic blood pressure to postural change. This latter observation strengthens the contention that the splanchnic area is of major importance in adjustment of the circulation to oppose the effect of gravity.

* Two additional cases of this series experienced definite symptoms of faintness or dizziness as the upright posture was reached.

† This factor probably contributes to inefficient respiratory and abdominal compensation for stasis of the blood mass in the splanchnic and dependent areas.

SUMMARY

The importance of adequate heart output, adequate blood volume and efficient adjustment of peripheral resistance in opposing the effect of gravity on the circulation is noted. Causes for failure of peripheral resistance to compensate for the upright posture are reviewed and the resultant pathologic physiology is discussed. The circulatory reactions in primary shock, emotional syncope and postural hypotension are compared. The danger accruing to the mechanism for postural adjustment from influences such as spinal cord injuries, too light anesthesia, chloroform, the forcing of ether anesthesia, high spinal anesthesia, asphyxia, excessive handling of the intestines, and severe operative procedures is reiterated. The differentiation between true postural hypotension and postural hypotension associated with Addison's disease by the response in pulse rate, is again presented, and the comparative rarity of both conditions in the literature is revealed. The trial of ephedrin in treatment of true postural hypotension is recommended. In searching for subjects who may exhibit defective postural adjustment, individuals exhibiting general weakness as a complaint and postural symptoms in their history are designated as the best potential group for study. The dominant rôle of the splanchnic area in opposing the effect of gravity appears, from the present review, to be strengthened.

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DISCUSSION

BURRELL O. RAULSTON, M. D. (University of Southern California, Los Angeles).—Doctor Ghrist emphasizes here a factor in symptomatology, if not in actual failure of health, that is frequently not recognized. When vasomotor instability is present to a degree sufficient to produce temporary symptoms of circulatory failure to the brain the condition may be recognized and dealt with according to the descriptions given in this paper. There must be a considerable number of patients who complain of lack of strength and endurance, lack of initiative, and lack of well-being, in whom a definite diagnosis is difficult and unsatisfactory, who suffer from mild degrees of the condition described here. A more thorough study of such patients in keeping with the ideas presented in this paper should be of value not only for the sake of a more accurate diagnosis but as a valuable aid in prescribing treatment. Undoubtedly many of the general measures used in treatment of patients who are diagnosed as having "general debility," "constitutional inferiority," and such indefinite conditions improve only because of some plan of management that corrects to some degree this condition of the vasomotor apparatus. If such patients could have the advantage of a more accurate diagnosis they might frequently be spared a considerable amount of drug therapy that is useless and often expensive.

AUDLEY O. SANDERS, M. D. (U. S. V. A., Diagnostic Center, Palo Alto).—Doctor Ghrist has rendered a definite service by repeatedly calling our attention to the clinical syndromes of arterial hypotension and by insisting that these syndromes often represent specific disease entities. In the past, far too little recognition has been given to these syndromes. In fact, they have seldom been considered as presenting separate clinical pictures in themselves. Rather, they have been merged into the confused and vague pictures of "neurasthenia," "effort syndrome," "visceroptosis," etc. It matters little what term may be used to identify the group of signs and symptoms characteristic of a disease entity; but it is exceedingly important that such a syndrome be generally recognized as evidence of some definite disease condition. Then, and then only, can advances be made in identifying the underlying pathology and in giving relief or help to the patient.

THOMAS G. INMAN, M. D. (2000 Van Ness Avenue, San Francisco).—Like many other problems in physiology, the causes which determine postural shifting of the blood quantum, or better, the reason for its not shifting equally in all individuals subjected to similar changes in body posture, may depend upon a number of influences acting together.

In a complex organism like the human body, it is impossible to estimate exactly the effect of a single factor acting upon a mobile structure such as is the blood. There are more than twenty variable factors constantly influencing the movement of this semi-fluid mass. It is possible only to give an approximate estimate of the effect of any one of them at a given time.

The fact that in certain otherwise healthy individuals untoward symptoms follow upon a change from the lying to the standing position, and that notable changes in blood pressure can be detected may, in the present state of our knowledge, be attributed to the effect of gravitation acting in an individual imperfectly equipped to maintain a stable equilibrium under varying changes in body position. The defect may lie in one instance in the vasomotor system, in another in atonic musculative, imperfect respiratory excursions, cardiac weakness, overactive psycho-visceral reflexes, etc. Perhaps it would be safer to look upon the postural blood pressure change as indicating a necessity for further search along the lines suggested by Doctor Ghrist.

Repeated observations lead to the belief that there is a certain type of individual in whom there exists a tardy adaptability to changes from the horizontal to the vertical position, and blood pressure determinations confirm the opinion that symptoms, when present, may be due to a defect in circulatory compensation. The long body, narrow thorax, small, central heart and limited diaphragm excursions point to the susceptible individual. In so far as the effect of gravity is concerned, some observers have suggested that the phenomenon may represent a lack of evolutionary adaptation to the vertical position; but opposed to this view is the fact that in a civilization in which many centuries of evolution are represented, blood ptosis, so called, is observed more frequently in those coming from the upper levels than in the more primitive groups. It may, indeed, be one of the penalties of civilization.

In the search for a permanently effectual therapy for these cases of constitutional postural hypotension too much stress may be placed upon medication directed toward increasing the activity of the propelling mechanism, forgetting that it is the return of the blood to the right heart that is the important matter. Thus, attempts to raise the blood pressure by stimulation of the heart only call for an expenditure of energy on the part of the circulatory system without obtaining a corresponding increase in the efficiency of the structures actually at fault.

Symptoms arising, directly or indirectly, from imperfect adjustment of the circulation of the lower half of the body are more common than is generally recognized and the timely studies of Doctor Ghrist will do much toward increasing our knowledge of the subject.